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# <Case Report>Breast Cancer and Recklinghausen's Disease

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CITATION:

NAKAMURA, MASAYUKI ...[et al]. <Case Report>Breast Cancer and Recklinghausen's Disease. 日本外科宝函 1998, 67(1): 3-9

ISSUE DATE:

1998-03-01

URL:

<http://hdl.handle.net/2433/202841>

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## 症 例

### Breast Cancer Associated with Recklinghausen's Disease: Report of a Case

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Received for Publication, Feb. 16., 1998

#### Abstract

A 49-year-old woman with Recklinghausen's disease presented to our department for investigation of a left breast lump, measuring 60 mm × 50 mm, which she had first noticed 6 months earlier, but had disregarded, believing it to be another manifestation of her Recklinghausen's disease. The lump was suspected to be malignant based on physical examination and ultrasonography. Biopsy and frozen sections subsequently confirmed a diagnosis of scirrhous carcinoma. A standard radical mastectomy was performed, followed by postoperative chemoendocrine therapy. However, lungs, liver, and bone metastasis, as well as a contralateral breast tumor, developed and she died 4 months after surgery.

#### Introduction

Recklinghausen's disease is an inherited disease mainly affecting the skin and nervous system that is rarely associated with malignant tumors. This report describes the case of a patient who developed breast cancer associated with Recklinghausen's disease.

#### Case Report

A 49-year-old woman had been diagnosed as having Recklinghausen's disease 25 years previously. She had the typical features of the disease, namely, numerous polypoid subcutaneous tumors and café au lait spots, but there was no family history of any similar disease. Although she had noticed a painless left breast lump 6 months prior to presentation, she had disregarded it, thinking it was another manifestation of her Recklinghausen's disease. She presented to our department on May 7, 1991 because of the pain associated with the gradually enlarging lump. Physical examina-

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索引用語: 乳癌, Recklinghausen 病

Key words: Breast cancer, Recklinghausen's disease



Fig. 1 Numerous tumors and café au lait spots were evident over the patients skin.

tion revealed an irregular hard tumor located in the upper outer quadrant of the left breast, measuring  $60\text{ mm} \times 50\text{ mm}$ . It was tender and there was nipple retraction, skin redness, and fixation to the underlying muscle. Two hard axillary lymph nodes were palpated. There were also a number of skin tumors and café au lait spots (Fig. 1). Ultrasonography showed an irregular heterogeneous

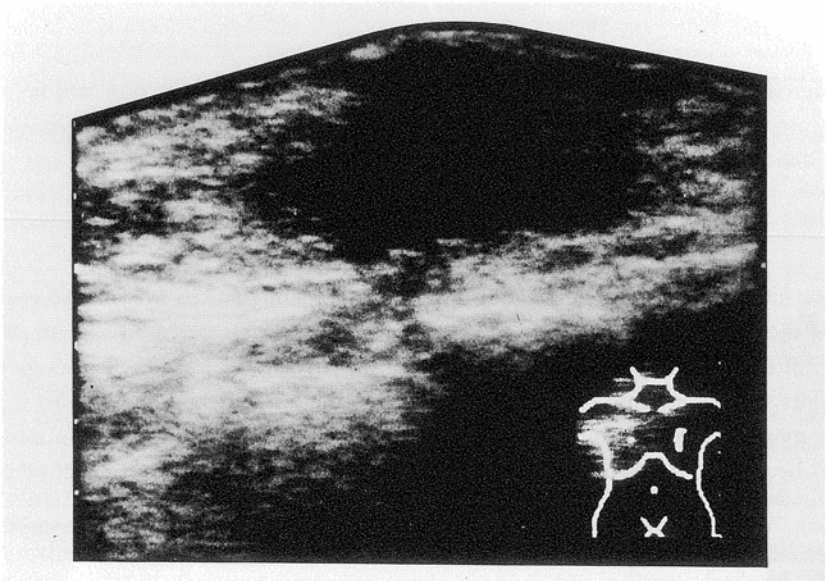


Fig. 2 An irregular heterogeneous hypoechoic mass was revealed by an ultrasonogram.

hypoechoic mass which was suspected to have invaded the skin and major pectoral muscle (Fig. 2). Her carcinoembryonic antigen (CEA), carcinoantigen 15-3 (CA 15-3), and tissue polypeptide antigen (TPA) levels were 4.2 ng/ml, 430 U/ml, and 1332.7 U/l, respectively, the normal values being  $<5.8$  ng/ml,  $\leq 30$  U/ml, and  $\leq 100$  U/l, respectively. Thus, a preoperative diagnosis of left breast cancer was made. The tumor was staged as T4bN1bM0, stage III<sub>b</sub><sup>1)</sup>. An excisional biopsy was per-

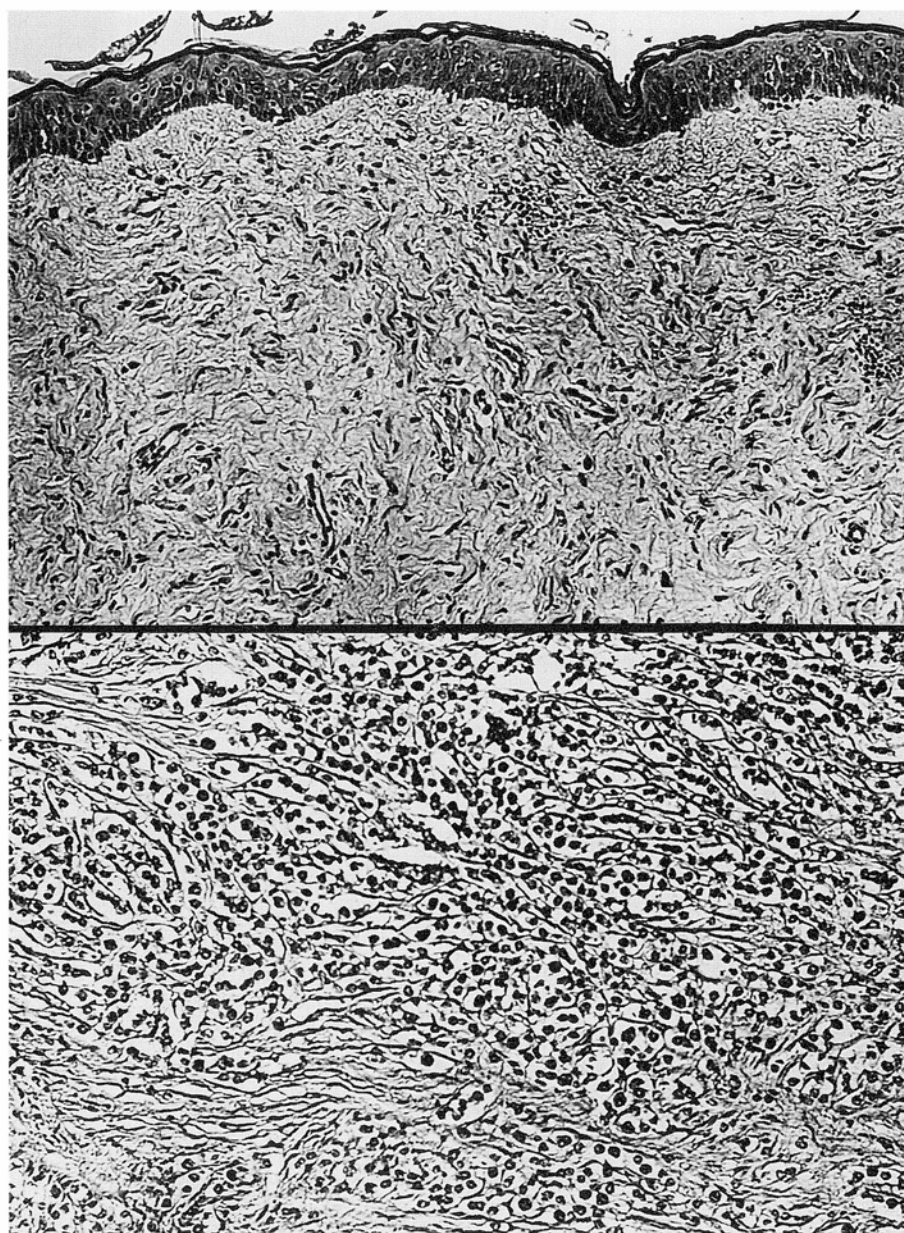


Fig. 3 Histological findings of the skin and breast tumors (H&E, original magnification  $\times 100$ ). The skin tumor was a neurofibroma (upper) and the breast tumor was scirrhous adenocarcinoma (bottom).

Table 1 Summary of cases of breast cancer associated with Recklinghausen's disease reported in Japan

Case	Year	Author	Age	Sex	Location	TNM-Stage	tnm-stage	Histology	Operation	Follow up from operation	Outcome
1	1972	Niimura	43	F	lt-CA	T4bNOMx-III b or IV	t3n0mx-II or IV	papillotubular ca.	Bt + Ax + Ic + Mj + Mn	2Y3m	death
2	1978	Ito	32	F	rt-?	TxNxMx-?	txnxmx-?	solid-tubular ca.	Bt + Ax	3Y9m	death (another disease)
3	1981	Maruo	59	F	rt-ABCDE	T4b or 4cNOM1-IV	t3or4nxm-IV	?	biopsy	1Y3M	death
4	1983	Gu	50	F	lt-C	T2aN1b or 2M0-II or III a	t2n1βm0-II	solid-tubular ca.	Bt + Ax + Ic + Mj + Mn	1Y5M	alive
5	1983	Hiraide	32	F	lt-EDCAB	T2aN1bM0-II	t2n0m0-I	solid-tubular ca.	Bt + Ax + Ic + Mj + Mn	9M	alive
6	1985	Yamamoto	60	F	lt-CD	T2aN1bM1-IV	t2n1m-IV	papillotubular ca.	Bt + Ax	8M	death
					rt-D	T2aN0M1-IV	t2n0m-IV	papillotubular ca.	Bt + Ax		
7	1985	Yoshizawa	71	F	rt-CD	T2aN0M0-II	t2n0m0-I	solid-tubular ca.	Bt + Ax + Ic + Mj + Mn	N. M.	alive
8	1989	Sako	58	F	rt-EABCD	T4bN2M1-IV	txnxm-IV	solid-tubular ca.	biopsy	5M	death
9	1989	Niiyama	38	F	rt-?	T1or2NxMx-?	0t1or2nxmx-?	ductal ca.	Bt	2Y	death (another disease)
10	1989	Konn	57	F	lt-D	T1aN1aM0-I	t1n0m0-I	papillotubular ca.	Bt + Ax + Ic + Mn	N. M.	N. M.
11	1990	Furuya	76	F	rt-?	T2NxMx-?	txnxm0-?	papillotubular ca.	biopsy	N. M.	alive
12	1992	Okamoto	72	F	rt-C	T2aN1aM0-II	t2n1αm0-II	scirrhus ca.	Bt + Ax + Ic + Mj + Mn	3Y	alive
13	1992	Nagase	46	F	lt-EABCD	T4cN1bM0-II	t3n1βor2m-IV	scirrhus ca.	Bt + Ax + Ic + Mj + Mn	N. M.	alive with bone metastasis
14	1992	Shingu	44	F	lt-ABCDE	T3aN0M0-III a	t2or3n0m0-I or II	spindle cell ca.	Bt + Ax + Ic + Mj + Mn	9M	death
15	1992	Ota	43	F	rt-DBE	T3aN1aM0-III a	txnxmx-?	scirrhus ca.	Bt + Ax + Ic + Mj + Mn	3Y	alive
16	1992	Ota	54	F	rt-D	T2N0M0-II	txnxmx-?	scirrhus ca.	Bt + Ax + Ic + Mj + Mn	3Y	alive
17	1993	Hirata	50	F	rt-CABDE	T3N0M0-III a	t3n0m0-III	mucinous ca.	Bt + Ax	58D	death (another disease)
18	1993	Aoki	58	F	rt-C	T2aN0M0-II	t1or2nxm0-?	squamous cell ca.	Bt	6Y4M	alive
19	1993	Aoki	32	F	rt-D	T1aN0M0-I	t1n1βm0-II	scirrhus ca.	Bq + Ax	1Y11M	alive
20	1994	Kobayashi	54	F	rt-E	T2aN1bM0-II	t2n1βm0-II	scirrhus ca.	Bt + Ax + Ic + Mj + Mn	5M	death
21	1994	Hayashi	25	F	lt-E	T1aN0M0-I	t1n0m0-I	papillotubular ca.	Bt + Ax	1Y	alive
					rt-D	T1aN0M0-I	t1n0m0-I	papillotubular ca.	Bt + Ax		
22	1994	Ishida	31	F	rt-CEAD	T3aN1bM0-III a	t3n1βm0-III	scirrhus ca.	Bt + Ax + Ic + Mj + Mn	3Y	alive
23	1994	Uematsu	48	F	rt-CDE	T2aN0M0-II	t2n0m0-I	papillotubular ca.	Bt + Ax	N. M.	alive
24	1995	Abe	44	F	lt-C + C	T2aN1bM0-II	t2n2m0-III	papillotubular ca.	Bt + Ax + Ic	N. M.	alive
25	1995	Inoue	45	F	lt-AC	T2N1bM0-II	t2n1βm0-II	papillotubular ca.	Bt + Ax + Ic + Mj + Mn	N. M.	alive with bone metastasis
26	1995	Sato	70	F	lt-CEA	T2aN0M0-I	t2n1βm0-II	papillotubular ca.	Bt + Ax	1Y6M	alive
27	1997	Nakamura	49	F	lt-CDBAE	T4bN1bM0-III b	t3n2m0-III	scirrhus ca.	Bt + Ax + Ic + Mj + Mn	4M	death

N. M.: Not mentioned

formed under general anesthesia and frozen sections revealed a scirrhous carcinoma. A standard radical mastectomy was then carried out according to the preoperative diagnosis, on May 23, 1991. Histological examination of paraffin sections revealed a scirrhous carcinoma (Fig. 3 bottom) which had invaded the overlying dermis and underlying major pectoral muscle. The axillary and infraclavicular lymph nodes were involved. Post-operatively the tumor was staged as t3n2m0, stage III<sup>1)</sup>. The skin tumor in the resected breast was histologically confirmed to be a neurofibroma (Fig. 3 upper). The breast cancer was negative for both estrogen receptor and progesterone receptor on enzyme immunoassay, the values being <6.9 fmol/mg protein, and <4.9 fmol/mg protein, respectively.

Despite two courses of chemotherapy consisting of cyclophosphamide, epirubicin and 5-fluorouracil, followed by doxifluridin and medroxy-progesterone acetate, she developed widespread metastasis in the lungs, liver, and bone, as well as a tumor in the contralateral breast, and died on October 8, 1991.

### Discussion

Recklinghausen's disease is an autosomal dominant disorder affecting about 1 in 4000 individuals, and 50% of patients have affected relatives. The gene for Recklinghausen's disease has recently been mapped to a site on chromosome 17, using a number of large kindreds. Multiple hyperpigmented areas, known as café au lait macules, and neurofibromas are characteristic. There are several possible manifestations of the disorder such as hypertension, scoliosis and other skeletal anomalies, macrocephaly, focal neurological deficits including impaired vision, ptosis, and optic atrophy, developmental disabilities, proptosis, Lisch nodules, short stature, signs of precocious puberty or hypogonadism, café au lait macules, and neurofibromas<sup>2)</sup>. Hence, consultation with numerous doctors is not uncommon.

Although the general consensus is that malignancies are rarely associated with Recklinghausen's disease, there is an increased incidence of sarcomas and leukemias, especially in childhood<sup>2)</sup>. However, KELLER and colleagues<sup>3)</sup> reported a case of adenocarcinoma of the pancreas associated with Recklinghausen's disease in a 27-year-old woman, while KAJIWARA and colleagues<sup>4)</sup> reported a case of adenocarcinoma of the gallbladder occurring in a 27-year-old man with this disease. There is possibly an increased incidence of a second malignancy in young people with Recklinghausen's disease because cancer of the pancreas or gallbladder is extremely uncommon in the normal young population.

To our knowledge, 26 cases of breast cancer associated with Recklinghausen's disease have been documented in the Japanese literature<sup>5-28)</sup>, including two cases<sup>10,23)</sup> of bilateral breast involvement, and ours is the 27th case report. All 27 patients were women varying in age from 25 to 76 years with an average age of 50.0 years. The T-factor was well documented in 27 sites<sup>5,7-28)</sup> of breast cancer and 9 of the 27 sites (33.3%) were beyond T3<sup>5,7,12,18-20,24)</sup>. The n-factor was described in 21 sites<sup>5,8-11,14,16-18,20-28)</sup> and 8 of these 21 sites (38.1%) were beyond n1<sup>8,17,21,22,24,26,27)</sup>. Of the 24 cases<sup>7-12,14-28)</sup> whose M-factor was described, 4 (16.7%) were M1<sup>7,10,12,17)</sup>. Most of the patients presented late, which was probably because the numerous skin tumors of neurofibromatosis hindered the discovery of breast lumps. In fact, our patient regarded the breast lump as another skin tumor.

Of the 27 patients, 5 (18.5%) were younger than 35-years-old<sup>6,9,21,23,24)</sup>; however, this incidence was higher than that reported by INAJI and colleagues<sup>29)</sup> whose incidence of breast cancer in the nor-

mal female population below 35-years-old was 6.7% among 1438 cases. Hence, there may be an increased risk of breast cancer in females with Recklinghausen's disease who are younger than 35 years old.

As the incidence of breast cancer is increasing in Japan, it stands to reason that breast cancer occurring simultaneously with Recklinghausen's disease will similarly increase. Thus, doctors at the several clinics these patients must attend regularly for their various problems must be diligent in excluding the possibility of a malignant breast tumor. If any suspicious mass is found, referral to an appropriate breast specialist is essential.

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和文抄録

## Recklinghausen 病に併存した乳癌の一例

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鈴木 敏

今回、我々は Recklinghausen 病（以下、R病）に併存した乳癌の一例を経験したので報告する。

症例は49歳、女性。左乳房に 60 mm×50 mm の腫瘤を自己触知して当科受診。彼女は6ヶ月前より、その腫瘤に気づいていたが、R病による腫瘤であろうと

考え、放置していた。触診、超音波検査上、乳癌が疑われた。術中迅速組織診断で乳癌の診断を得て、定型的乳房切除術を施行した。術後、内分泌・化学療法を施行したが、肺・肝・骨転移及び対側乳房の腫瘤が出現し、術後4ヶ月めに死亡した。